REMARKS/ARGUMENTS

1. Status

Claims 1, 2, 5-10 and 12-18 are pending. Claims 1 and 14-17 have been amended. New claims 19 and 20 have been added. Therefore, upon entry of this amendment, which is respectfully requested, claims 1, 2, 5-10 and 12-20 will be pending.

The undersigned thanks the Examiner for a telephone interview conducted on February 12, 2004. The Examiner indicated that she would send an interview summary with the next Patent Office paper. As such, no summary is included herein.

2. Claim Rejections - 35 USC §112:

New Matter; §112, first paragraph

Claims 1, 2, 5-10 and 12-18 have been rejected under 35 USC §112, first paragraph, as failing to comply with the written description requirement. In particular, it was stated that this was a new matter rejection as the (then-amended) claims contain subject matter which was not described in the specification in such a way as to reasonable convey to one skilled in the art that the inventors had possession of the claimed invention at the time of filing of the application.

Applicants respectfully disagree. The substantive amendments made to the claims in the prior response were fully supported by the specification. Although the claims have since been amended herein, support for the previous amendments will first be pointed out, followed by support for the current amendments.

The claims were amended to recite, and the specification teaches, a computer implemented method of identifying whether a test subject is suffering from one or more systemic autoimmune diseases (SADs). The present invention may be implemented with the aid of computer software in a computer based system such as a medical decision support system. See, *e.g.*, page 3, lines 14-19 and page 6, line 32 to page 7, line 2. Identifying whether the test subject is suffering from one or more SADs will be discussed below in response to a specific comment in the Rejection. Briefly, however, identifying *whether* the test subject is suffering from one or

more SADs follows inherently from an indication that the test subject is suffering from *none or one or more* specific SADs as is taught by the specification.

The claims were also amended to recite "receiving a test data set for the test subject," and "storing a plurality of reference data sets". An example of support for these limitations can be found in the specification at page 4, line 30 to page 5, line 5 and page 4, lines 16 to 19. The claims were further amended to recite "comparing the test data set and the reference data sets by applying a k-nearest neighbor process". An example of support for this limitation can be found at page 5, lines 6 to 8, and the paragraph beginning at page 5, line 14 for a discussion of k-nearest neighbor (KNN) processing.

Additional pertinent disclosure and teaching of the amendments discussed above and others can be found at page 4, line 7 to page 6, line 2, and page 6, line 32 to page 7, line 5.

Additional amendments have been made herein. Support for the various amendments made herein can be found in the above sections. For example, support for amendments to the claims to recite that the test data set and each reference data set is obtained by subjecting a biological sample to a set of one or more tests can be found, for example, at page 5, lines 1 to 5, page 4, lines 15 to 19, and page 10, lines 10 to 14. Further, additional support for amendments to claim 1 to recite that the reference data sets include "i) reference data sets obtained for each of said one or more systemic autoimmune diseases by subjecting biological samples of reference subjects, each known to have one of said one or more systemic autoimmune diseases, to said set of one or more tests, and ii) reference data sets obtained by subjecting biological samples of reference subjects known to not have one of said one or more systemic autoimmune diseases to said set of one or more tests," can be found at page 4, lines 10-15. Further, support for amendments to the claims to recite "none" with regard to a statistically derived decision indicating whether the test subject is suffering from none or one or more of the SADs, can also be found, for example, at page 4, lines 11 to 16. For specific teaching in the context of a KNN process, support is also found at page 5, line 19-30; *e.g.*, if the k nearest points, or a subset, are associated with reference samples that were known to not have any of the diseases, the decision will indicate "none". Support for claim 17 to recite that each of the

reference data sets has a "specific association" with one or more of said SADs can be found at page 4, lines 24-26. Examples of support for new claims 19 and 20 can be found at page 3, lines 26-28 and page 9, lines 11-14.

It was stated in the rejection that the claims require determining whether the test subject is suffering from one or more autoimmune diseases but not determining which ones, whereas the previous claims required identification of the particular autoimmune disease(s). The present invention, as set forth in the specification, teaches a system for identifying particular SADs from a set of SADs sought to be investigated for the test subject. The training set with which a test sample is compared includes data associated with the SADs sought to be investigated for a particular patient or patients. The training set is made up of reference samples that have disease conditions that are known as well as samples that are known to be disease free. See, page 4, lines 10-16. Each reference sample is therefore associated with, none, one or more of the systemic autoimmune diseases. When the test data set is statistically compared with the training data set using a nearest neighbor process, or algorithm, such as a k-nearest neighbor (KNN) process, or algorithm, as disclosed (for example, beginning at page 5, line 14), a determination of one or more particular diseases may be achieved. The KNN algorithm processes the training data sets and test data set as data points in an N-dimensional space, where N is the number of test values (e.g., antibody test levels) obtained for each sample. The disease(s) associated with the k nearest data points (from the training sets) that are closest (based on a numeric distance metric) to the test data point are then identified as a disease which is present in the patient sample from which the test data point is derived. If the k nearest data points are associated with more than one disease, the diagnosis for each of the diseases may be indicated. In such a system, if the k nearest data points are associated with none of the diseases (e.g., if many or all of the k nearest test data points were derived from samples from subjects known to be disease free), then the diagnosis would be "none". Inherent in this is a system that provides an indication of whether a subject is suffering from one or more of the SADs; that is, a determination that a patient is suffering from none, or one or more of the SADs that were sought

to be investigated for the patient(s) inherently, and logically, includes a determination of whether the subject is suffering one or more of the SADs.

It was also stated that the specification does not appear to disclose the concept of a "k-nearest neighbor process." Applicants respectfully disagree. Although the claims have been amended herein to recite a "k-nearest neighbor algorithm", Applicants respectfully assert that "process" in the context of a computer implemented method is similar, if not identical to, an "algorithm". In general, the present invention uses a k-nearest neighbor algorithm to calculate numeric distances between the training set data points and the test data point. Different k-nearest neighbor processes may rely on different numeric metrics distance comparisons, however, implementation of, or modification of, a specific k-nearest neighbor algorithm to process the data sets as described in the specification is readily within the ability of one skilled in the art.

It was also pointed out that claims 1 and 17 appear to be directed to identical methods. It is respectfully asserted that these two claims were directed to *similar* methods. Nonetheless, this comment is now moot in light of the current amendments to these claims, which remain similar in scope, yet not identical. For example, claim 1 now also recites the additional limitation of identifying which of the SADs the test subject is suffering from, and also "none" in reference to the SADs a reference subject is known to suffer from.

Enablement; §112, first paragraph

This rejection for lack of enablement is respectfully traversed.

It is stated in the rejection that "the specification does not associate any antigen (or antibody) with any particular disease with respect to presence (or absence) and amounts." It is further stated in the rejection that there is no guidance in the specification "as to determining unknown autoantibodies related to the named systemic autoimmune diseases." It is respectfully submitted that the present invention involves neither the association of particular antigens or antibodies with particular diseases nor the determination of unknown antibodies related to particular diseases.

The present invention is not concerned with discovering antibodies, nor of associating particular antibodies with diseases. Instead, the invention resides in, and claim 1, for

example, expressly recites, comparing the test data set and the reference data sets which include reference data sets obtained for each of the one or more systemic autoimmune diseases by subjecting biological samples of reference subjects, each known to have one of the one or more systemic autoimmune diseases, to said set of one or more tests, and reference data sets obtained by subjecting biological samples of reference subjects known to not have one of the one or more systemic autoimmune diseases to said set of one or more tests. As taught at page 5, lines 1 to 5, for example, the test data set is based on samples subjected to the same tests as the reference sample. And this is reflected in the claims wherein it is recited that the reference data sets are each obtained by subjecting a sample of a reference subject "to said set of one or more tests," (emphasis added) with said set of tests referring to the set of tests applied to the sample of the test subject. There is therefore no correlation between antibodies and diseases, only between one test data set and a plurality of reference data sets and the diseases with which they are associated.

And there is no determination of unknown antibodies; whichever antibody tests are decided to be used are used for both the reference data sets and the test data set. It is irrelevant for the purposes of the claimed invention what antibody tests and therefore also which antibodies are used for the tests, so long as there is some amount of consistency in the tests that are applied to the reference samples and the test sample to derive the data sets. The use of particular antibodies and particular antibody tests may lead to improved results (see, *e.g.*, page 8, lines 9-12), however, the invention and the pending independent claims are not limited to the use of particular antibodies or antibody tests. Nor is such use necessary as any antibodies and antibody tests known to one skilled in the art may be used. For example, the Peter *et al.* text referenced on page 7 of the specification is cited merely to indicate some of the autoimmune antibodies that are known to exist and that a large number of these antibodies have known antigens. Peter *et al.* is cited only to indicate the state of the art, and is not a disclosure of the invention or of elements, otherwise unknown, that are critical or essential to the implementation of the invention. The incorporation of Peter *et al.* by reference is therefore not improper. Further, it would be routine to identify additional antibodies that could be used with the present invention. For example, as specific antibodies are discovered, the tests to identify such antibodies could be used on the reference samples and the test sample to add an extra dimension

to the N-dimensional data being processed according to the present invention. It is routine to one skilled in the art of antibody discovery to discover new antibodies as well as new techniques for such discovery. To those artisans, such matters of investigation are indeed routine, and are also outside the scope of the presently claimed invention.

Also, there is also no assigning of presence, absence or amounts of any particular antibodies to any particular disease since the reference sets are already identified as to the diseases in which they appear, as described, for example, in the specification at page 4, lines 15 to 29. Again, each reference data set is associated with a particular disease or none. For example, as taught at page 4, lines 24 to 26, each point is labeled as to the particular disease that is associated with its source. And from page 4, lines 11 to 15, each reference data set may be associated with a specific disease or no disease. The levels of the antibodies are those levels that are provided by the tests used, and the same or similar tests are used for both the test subject and the reference subjects as discussed above.

The rejection also states that "the specification [does not] disclose how discrimination between different autoimmune diseases, particularly with those that involve overlapping autoantibodies, is to be implemented." To the contrary, the specification does indeed disclose how such discrimination is achieved. Discrimination between the various autoimmune diseases is achieved by the KNN process as described at the paragraph beginning on page 5, line 14. For example, the disease that is associated with the k nearest (reference) data points is that which is identified as being present in the test sample, and if more than one disease is associated with the k nearest (reference) data points then the diagnosis is for each of the diseases (or none if the reference data points are associated with reference samples known to be disease free). Additional refinements are also presented in the cited paragraph, such as, for example, to determine a confidence level of the diagnosis. Again, it is not particularly relevant what the antibodies are, just that each of the data sets have been subjected to the same antibody testing.

Accordingly, it is respectfully asserted that the present specification provides sufficient guidance to enable one skilled in the art to implement the claimed invention. Again, the presently claimed invention is directed to a method of processing the data as recited therein.

There is no recitation in the claims of discovering antibodies or of associating antibodies with particular diseases. The specification supplies more than adequate support for one skilled in the art to implement a KNN algorithm using the data sets as recited in the claims. Further, the specification supplies more than adequate support for a useful structure and composition of the data sets themselves (e.g., training or reference data sets and test data set) for use in a KNN algorithm. Furthermore, the training set and the test set include values for known (now or in the future) autoimmune antibodies. The specification explains this thoroughly and adequately, citing a large number of examples of autoimmune antibodies. The specification is not a mere "invitation to experiment" as it is characterized by the Office Action. The specification is a teaching that when combined with the existing knowledge and the routine level of skill among data processors and statisticians provides a fully enabling disclosure to support the claims. To the extent one skilled in the art would need to make assumptions as to what specific data would be used, such basic assumptions are a routine matter for one skilled in the art. For example, one skilled in the art would easily be able to implement data filtering, skew adjustment and normalization techniques as may be desired without undue experimentation.

Accordingly, the rejection of the claims under 35 USC §112, first paragraph, is respectfully traversed.

Rejection to claim 16 under §112, second paragraph

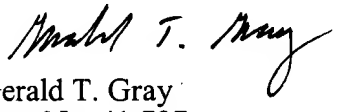
Claim 16 was rejected as being indefinite. In particular, it was stated that claim 16 is confusing and inconsistent in reciting "said one or more systemic autoimmune diseases consists of systemic lupus erythmatosus." Appropriate correction has been made; claim 16 has been amended herein to recite "said one or more systemic autoimmune diseases includes systemic lupus erythmatosus."

CONCLUSION

In view of the foregoing, Applicants believe all claims now pending in this Application are in condition for allowance. The issuance of a formal Notice of Allowance at an early date is respectfully requested.

If the Examiner believes a telephone conference would expedite prosecution of this application, please telephone the undersigned at 925-472-5000.

Respectfully submitted,



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Attachments
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